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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,728	12/28/2001	Albert H. Olivencia-Yurvati	073314.0102	6388

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,728	OLIVENCIA-YURVATI ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *7-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/03/2004 has been entered.

Status of claims

Claims 7-17 as amended {3/30/2004} are pending and under examination.

Claims 1-6 and 18 were withdrawn {5/05/2003} as directed to non-elected invention without traverse {3/03/3003}.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 7-17 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/02653 [IDS-6 ref. H] taken with Rao et al. [IDS-6 ref. M], US 4,988,515 [IDS-4 ref. B] and Tejero-Taldo et al. [IDS-4 ref. RR] as explained in the prior office action and repeated herein.

Claims are directed to a process for performing cardiopulmonary bypass surgery by administering a composition or a cardioplegia solution comprising pyruvate, NaCl, KCl, glucose, insulin, CaCl2 and lidocaine in amounts within the following ranges 0.2-50 mM pyruvate, 0-250 mM NaCl, 10-250 mM KCl, 0-200 mM glucose, 0-200 U/L insulin, 0-20 CaCl2 mM and 0-2 g/L

lidocaine to the heart of a human patient in order to arrest the heart during the surgery. Some claims are further drawn to dilution of cardioplegia composition with whole blood prior administration at the ratio blood to solution such as 0.1-20 to 1. Some claims are further drawn to the intended effects of administration including protection of the heart from injury resulting from ischemia, rapid recovery of mechanical function, stabilization of heart energy reserves, antioxidant action and inotropic support.

The cited references are relied upon as explained in the prior office action and repeated herein.

WO 93/02653 teaches a process for performing cardiopulmonary bypass surgery comprising heart arrest during cardiac operations by administering directly to the heart of human patient a cardioplegia composition or a cardioplegia emulsion/solution (example C, pages 19-20). The cardioplegia emulsion of the cited WO document comprises components of crystalloid solutions including 100-150 mM NaCl, 5-20 mM KCl, 0.5-30 mM CaCl2, 5-300 mM glucose, pyruvate 5-100 mM and 0.1-0.5 mM lidocaine (table 1, page 11) wherein the concentrations of components are within the ranges as required by the presently claimed method. The emulsion in the clinical open-heart surgery as disclosed by the cited WO 93/02653 incorporates pyruvate as an optional ingredient and one of metabolic substrates (table 1).

The cited WO 93/02653 is lacking disclosure related to incorporation of insulin in the cardioplegia composition during cardiopulmonary bypass surgery including heart arrest.

However, the reference by Rao et al teaches a process for performing cardiopulmonary bypass surgery including heart arrest wherein in the method of Rao the cardioplegia solution comprises 10 IU/L insulin (abstract) as a beneficial component that provides for myocardial

metabolic and functional recovery (abstract) of patients in need of cardiopulmonary bypass surgery.

Thus, both cited references WO 93/02653 and Rao et al disclose methods for performing cardiopulmonary bypass surgery including heart arrest by administering a composition/cardioplegia solution with the presently claimed ingredients within the presently claimed ranges. However, the cited WO 93/02653 and Rao et al are silent with regard to a dilution of the cardioplegia solution with blood before administration of the cardioplegia solution.

However, US 4,988,515 teaches a process for performing cardiopulmonary bypass surgery wherein the cardioplegia solution is mixed with blood in the ratio blood to concentrated solution 4:1 (col. 4, lines 15-20). The cited patent also suggests the use of the pyruvate containing cardioplegia solution (col. 4, line 5) for performing cardiopulmonary bypass surgery.

In addition, the cited reference by Tejero-Taldo et al. [IDS-4 ref. RR] is relied upon to demonstrate the beneficial effects of the pyruvate containing compositions in cardiac operations. For example: the reference teaches an antioxidant action of the pyruvate containing composition or cardioplegia solutions in the method comprising heart perfusion with cardioplegia solution (abstract) and it also discloses the role of pyruvate as natural fuel for the cardiac muscle, the role of pyruvate to potentate inotropic response and to prevent the energy depletion (introduction).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine chemical components of cardioplegia solution including pyruvate, NaCl, KCl, glucose, insulin, CaCl2 and lidocaine at concentration as taught and/or suggested by the cited references WO 93/02653 and Rao et al. in the method for

performing cardiopulmonary bypass surgery in patients including human patients with a reasonable expectation of success because it is well known that it is prima facie obvious to combine ingredients which are taught by the prior art to be useful for the same purpose of performing cardiopulmonary bypass surgery in human patients in order to form a composition which is useful for the same purpose. The idea for combining the known components flows logically from their having been used separately in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). One of skill in the art would have been motivated to incorporate pyruvate in the cardioplegia solution in the method for performing cardiopulmonary bypass surgery in patients including human patients for the expected benefits in protecting the heart from injury resulting from ischemia, rapid recovery of mechanical function, stabilization of heart energy reserves, antioxidant action and inotropic support because these beneficial effects of pyruvate are well known in the prior art as adequately demonstrated by the disclosure of Tejero-Taldo et al. It is considered to be within the purview of one having ordinary skill in the art to adjust the final concentration of therapeutically effective amounts of cardioplegia solution by mixing blood with a concentrated cardioplegia solution in the method for performing cardiopulmonary bypass surgery in human patients as taught by US 4,988,515. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 3/03/2004 have been fully considered but they are not persuasive.

With regard to the cited WO 93/02653 applicants argue that the cited document taken as the whole teaches the use of a fluorocarbon emulsion (page 5, par. 1) but not the use of a crystalloid vehicle alone. Nevertheless, the crystalloid vehicle is also administered in the same method of surgery and the crystalloid vehicle is optionally fortified with pyruvate as disclosed by the cited WO 93/02653. Although the major focus of the invention of WO 93/02653 is on the use of fluorochemicals, the reference teaches the use of pyruvate as optional component of cardioplegia solution (table 1) for the same type of surgery as presently claimed by applicants.

The prior art references are relevant as prior art for all they contain and the nonpreferred or the optional embodiments constitute prior art. See MPEP 2123. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998). "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33,216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006,1009, 158 USPQ 275, 277 (CCPA 1968)). Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423

(CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

With respect to one of the secondary references {Tejero et al.} applicant argues that in the particular disclosure it teaches the animal models but not the human models (response pages 5-6). Yet, this reference is relied upon to demonstrate that the physiological role of pyruvate as a natural fuel for cardiac muscle is well established and known. Thus, the applicants' argument as drawn to unpredictability of the pyruvate role in human model is not found persuasive because pyruvate is universal metabolic substrate for all animals including humans and, thus, the beneficial effects of pyruvate at the very least as cardiac muscle fuel is reasonably expected to be the same for all animal applications/models including human applications/models.

The data from animal testing is generally sufficient to support the therapeutic utility of chemical compounds. See MPEP 2107.03. (III, IV). Moreover, all ingredients in the cardioplegia solution that are required in the presently claimed method have been taught and/or suggested for human applications as adequately demonstrated by WO 93/02653 and Rao et al..

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-100.

Vera Afremova

AU 1651

April 14, 2004

V. Afremova

VERA AFREMOVA

PATENT EXAMINER